Chemical Name: Diphacinone

PC Code: 067701

CAS No: : 82-66-6

MRID: N/A

ECOTOX Record Number: 150802

Citation: Rattner, B.A., K.E. Horak, S.E. Warner and J.J. Johnston. 2010. Acute toxicity of diphacinone in Northern bobwhite: Effects on survival and blood clotting. Ecotoxicology and Environmental Saftety. 73:1159-1164

Purpose of Review: Rodenticide Evaluation

Date of Review: ~~11/01/11~~ 5/10/12 MW

Description of Use in Document (QUAL, QUAN, INV):

Qualitative

Summary of Study Findings:

The study authors performed two experiments: determining an acute oral LD_{50} of diphacinone to Northern bobwhite quail (*Colinus virginianus*) and also a series of clotting assays. The reviewer only evaluated the data presented in the acute oral LD_{50} determination and not the clotting assays. The reviewer calculated an LD_{50} of 1946 mg/kg (95% CI: 1603--2383) with a slope of 5.51 (95% CI: 3.45—7.58).

Bobwhite were obtained from R&R Game Birds (Lamar, CO) and housed individually in indoor pens (2806 cm^2/bird) at the National Wildlife Research Center. They were maintained using a 12hr photoperiod at temperatures ranging from 18—21^{0}C and provided Purina Game Maintenance Chow® Product 5440 and water *ad libitum*.

Birds weighed from 149—224g and were gavaged with technical diphacinone (99% a.i.) with soybean oil used as a carrier. Due to diphacinone's low solubility, it was administered as slurry in vegetable oil. Although the birds were dosed and then observed for 14 days, this experiment took six weeks since diphacinone doses were selected through an iterative process not described in this article. It is unclear from the article whether controls were used throughout the 6-week time period (though the reviewer assumed that they were, and inferred that the same control birds were used three times over the six week study period). Birds were exposed to diphacinone at nominal rates of 0, 917, 965, 1033, 2065, 2868 and 3666 mg/kg-bw. Some doses were administered as a split-dose over a 24-h period (nominal exposure of 1033 and 2065 mg/kg administered as two doses, nominal exposure of 2868 mg/kg administered as three doses and nominal exposure of 3666 mg/kg administered as four doses. For the split-dose concentrations, it is unclear how much time elapsed between dosings. The controls were dosed with the carrier

alone 1-3 times/day. 9 or 10 bobwhites were dosed at each treatment level with an approximately equal distribution of sexes at each dose.

Mortality data is presented in Table 1. The LD_{50} and slope were determined using the probit method in SAS. The study author's determined an LD_{50} of 2014 mg/kg (95% CI: 1620—2475 mg/kg) with a slope of 9.92 ± 2.27. Observed sublethal effects include lethargy and ruffled feathers. Necropsy showed bruising in the breast and back regions of birds in the highest concentrations, though the authors reported that there was no evidence of frank internal or external bleeding. Controls did not exhibit overt signs of toxicity.

Nominal Dose (mg/kg)	# Doses[1]	Mortality (#dead/#tested)
0	1-3	0/9
917	1	1/10
965	1	1/9
1033	2	0/10
2065	2	3/10
2868	3	9/10
3666	4	10/10

[1]To reach nominal concentration; applied within a 24-hr period

The reviewer's results, calculated using the probit method in Toxanal2009, were similar with the study authors' results (Appendix I), however the reviewer's results indicated a slightly more sensitive LD_{50} of 1946 mg/kg (95% CI: 1603—2383) with a shallower slope of 5.51 (95% CI: 3.45—7.58). However, the use of multiple dosings over a 24-hr period to reach the nominal concentrations for the four highest treatment levels may impact the ratio of the amount of test material absorbed through the gut walls relative to the amount of test material passed quickly through the digestive system and eliminated in those concentrations. Consequently, the calculated LD_{50} value could be higher or lower than would be determined based on a single dose.

Rationale for Use:

Provides an acute oral LD_{50} for northern bobwhite quail exposed to diphacinone, which can be used to characterize the toxicity of diphacinone to avian organisms.

Limitations of Study:

- Not all concentrations were tested at the same time, but instead were tested at three different time intervals within a six week study period. It appears controls were used throughout the six week study period.
- The study authors used a divided dose methodology in the four highest treatment levels where the dose was divided and applied over a 24-hour period. This may impact the ratio of the amount of test material absorbed through the gut walls relative to the amount of test material passed quickly through the digestive system and eliminated in these treatment levels. Depending on the effect of the divided dosing on adsorption, the

calculated LD_{50} could be higher or lower then would be determined based on a single dose.

- Data regarding food consumption and body weight gain were not provided.
- A Certificate of Analysis was not provided.

Description of Use in Document (QUAL, QUAN, INV):

Qualitative

Primary Reviewer: Michael Wagman, Biologist, EPA/ EFED/ERB6 5/10/12

Appendix I

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     CONC.          NUMBER          NUMBER           PERCENT          BINOMIAL
                    EXPOSED         DEAD               DEAD           PROB.(PERCENT)
      3666          10              10                 100             9.765625E-02
      2868          10              9                   90             1.074219
      2065          10              3                   30             17.1875
      1033          10              0                    0             9.765625E-02
      965            9              1             11.11111             1.953125
      917           10              1                   10             1.074219

     THE BINOMIAL TEST SHOWS THAT 1033 AND 2868 CAN BE
     USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
     CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
     ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

     AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 2288.018

     RESULTS CALCULATED USING THE MOVING AVERAGE METHOD
        SPAN      G           LC50          95 PERCENT CONFIDENCE LIMITS
      5         .1049589      1914.41       1626.226       2296.883

     RESULTS CALCULATED USING THE PROBIT METHOD
     ITERATIONS              G               H            GOODNESS OF FIT PROBABILITY
         6                    .1401166       1                          .1652314

     SLOPE    =               5.513462
     95 PERCENT CONFIDENCE LIMITS = 3.449654     AND     7.57727

     INTERCEPT=-18.13459

     LC50 =     1946.018
     95 PERCENT CONFIDENCE LIMITS =  1603.345 AND  2382.568

              LC25 =          1468.283
     95 PERCENT CONFIDENCE LIMITS =  1122.782 AND  1766.987

              LC10 =          1139.456
     95 PERCENT CONFIDENCE LIMITS =  779.4861 AND  1411.27

              LC05 =          979.0488
     95 PERCENT CONFIDENCE LIMITS =  620.2601 AND  1246.189
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